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Applicant : Taka-Aki Sato

Serial No. : 09/327,750

Examiner: Not Me  
TECH CENTER 1600/2900

Filed : June 7, 1999

Group Art Unit: 1632

For : GENE ENCODING NADE, p75<sup>NTR</sup> - ASSOCIATED CELL  
DEATH EXECUTOR AND USES THEREOF

1185 Avenue of the Americas  
New York, New York 10036  
December 29, 1999

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

Applicants submit herewith an Information Disclosure Statement under 37 C.F.R. §1.56.

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following disclosures:

1. Baeuerle, P. A. & Henkel, T., (1994) Function and Activation of NF-kappa B in the Immune System. Annu. Rev. Immunol. 12, 142-179 (**Exhibit 1**);
2. Barrett, G. L. & Bartlett, P. F., (1994) The p75 Nerve Growth Factor Receptor Mediates Survival or Death Depending on the Stage of Sensory Neuron Development. Proc. Natl. Acad. Sci. USA 91, 6501-6505 (**Exhibit 2**);
3. Breeden, L. & Nasmyth, K., (1985) Regulation of the Yeast HO Gene. Cold Spring Harbor Symp. Quant. Biol. Vol. L, 643, 650 (**Exhibit 3**);

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4. Bunone, G., Mariotti, A., Compagni, A., Morandi, E. & Della Valle, G., (1997) Induction of Apoptosis by p75 Neurotrophin Receptor in Human Neuroblastoma Cells. Oncogene 14, 1463-1470 (**Exhibit 4**);
5. Carter, B. D., Kaltschmidt, C., Kaltschmidt, B., Offenhauser, N., Bohm-Matthaei, R., Baeuerle, P. A. & Barde, Y. A., (1996) Selective Activation of NF-kappa B by Nerve Growth Factor Through the Neurotrophin Receptor p75. Science 272, 542-545 (**Exhibit 5**);
6. Casaccia-Bonofil, P., Carter, B. D., Dobrowsky, R. T. & Chao, M. V., (1996) Death of Oligodendrocytes Mediated by the Interaction of Nerve Growth Factor with its Receptor p75. Nature 383, 716-719 (**Exhibit 6**);
7. Chao, M. V. & Hempstead, B. L., (1995) p75 and Trk: a Two-receptor System. Trends Neuroscience 18, 321-326 (**Exhibit 7**);
8. Ciechanover, A., (1998) The Ubiquitin-proteasome Pathway: on Protein Death and Cell Life. The EMBO Journal 17(24), 7151-7160 (**Exhibit 8**);
9. Datta, R., Banach, D., Kojima, H., Talanian, R. V., Alnemri, E. S., Wong, W. & Kufe, D. W., (1996) Activation of the CPP32 Protease in Apoptosis Induced by 1-beta-D-Arabinofuranosylcytosine and Other DNA-Damaging Agents. Blood 88, 1936-1943 (**Exhibit 9**);
10. Feinstein, E., Kimchi, A., Wallach, D., Boldin, M. & Varfolomeev, E., (1995) The Death Domain: A Module Shared by Proteins with Diverse Cellular Functions. Trends

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Biochem. Sci. 20, 342-344 (**Exhibit 10**);

11. Fernandes-Alnemri, T., Litwack, G. & Alnemri, E. S., (1994) CPP32, a Novel Human Apoptotic Protein with Homology to Caenorhabditis Elegans Cell Death Protein Ced-3 and Mammalian Interleukin-1 Beta-converting Enzyme. J. Biol. Chem. 269(49), 30761-30764 (**Exhibit 11**);
12. Fields, S. & Song, O., (1989) A Novel Genetic System to Detect Protein-protein Interactions. Nature 340, 245-246 (**Exhibit 12**);
13. Frade, J. M., Rodriguez-Tebar, A. & Barde, Y. A., (1996) Induction of Cell Death by Endogenous Nerve Growth Factor Through its p75 Receptor. Nature 383, 166-168 (**Exhibit 13**);
14. Gavrieli, Y., Sherman, Y. & Ben-Sasson, S. A., (1992) Identification of Programmed Cell Death in situ via Specific Labeling of Nuclear DNA Fragmentation. J. Cell Biol. 119(3), 493-501 (**Exhibit 14**);
15. Gietz, D., Jean, A. S., Woods, R. A. & Schiestl, R. H., (1992) Improved Method for High Efficiency Transformation of Intact Yeast Cells. Nucl. Acids Res. 20(6), 1425 (**Exhibit 15**);
16. Ito, H., Fukuda, Y., Murata, K. & Kimura, A., (1983) Transformation of Intact Yeast Cells Treated with Alkali Cations. J. Bacteriol. 153(1), 163-168 (**Exhibit 16**);
17. Johnson, D., Lanahan, A., Buck, C. R., Sehgal, A., Morgan, C., Mercer, E., Bothwell, M. & Chao, M., (1986) Expression

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and Structure of the Human NGF Receptor. Cell 47, 545-554  
(Exhibit 17);

18. Kaplan, D. R. & Miller, F. D., (1997) Signal Transduction by the Neurotrophin Receptors. Curr. Opin. Cell Biol. 9, 213-221 (Exhibit 18);
19. Khursigara, G., Orlinick, J. R. & Chao, M. V., (1999) Association of the p75 Neurotrophin Receptor with TRAF6 J. Biol. Chem. 274(5), 2597-2600 (Exhibit 19);
20. Lezoualc'h, F., Sagara, Y., Holsboer, F. & Behl, C., (1998) High Constitutive Nf-kappa B Activity Mediates Resistance to Oxidative Stress in Neuronal Cells. J. Neurosci. 18(9), 3224-3232 (Exhibit 20);
21. Liepinsh, E., Ilag, L. L., Otting, G. & Ibanez, C.F., (1997) NMR Structure of the Death Domain of the p75 Neurotrophin Receptor. The EMBO Journal 16(16), 4999-5005 (Exhibit 21);
22. Murphy, T., Cleveland, M., Kulesza, P., Magram, J., Murphy, K., (1995) Regulation of Interleukin 12 p40 Expression through an NF-kB Half-Site. Molecular and Cellular Biology 15(10), 5258-5267 (Exhibit 22);
23. Nakielnny, S. & Dreyfuss, G., (1997) Nuclear Export of Proteins and RNAs. Curr. Opin. Cell Biol. 9, 420-429 (Exhibit 23);
24. Pan, J., McEver, R. P., (1995) Regulation of the Human P-selectin Promoter by Bcl-3 and Specific Homodimeric

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Members of the NF- $\kappa$ B/Rel Family. J. Biol. Chem. 270(39),  
23077-23083 (**Exhibit 24**);

25. Pietravalle, F., Lecoanet-Henchoz, S., Blasey, H., Aubry, J. P., Elson, G., Edgerton, M. D., Bonnefoy, J. Y. & Gauchat, J. F., (1996) Human Native Soluble CD40L is a Biologically Active Trimer, Processed Inside Microsomes. J. Biol. Chem. 271(11), 5965-5967 (**Exhibit 25**);
26. Rabizadeh, S., Oh, J., Zhong, L., Yang, J., Bitler, C. M., Butcher, L. L. & Bredesen, D. E., (1993) Induction of Apoptosis by the Low-affinity NGF Receptor. Science 261, 345-348 (**Exhibit 26**);
27. Rapp, G., Freudenstein, J., Klaudiny, J., Mucha, J., Wempe, F., Zimmer, M. & Scheit, K. H., (1990) Characterization of Three Abundant mRNAs from Human Ovarian Granulosa Cells. DNA and Cell Biol. 9(7), 479-485 (**Exhibit 27**);
28. Schlegel, J., Peters, I., Orrenius, S., Miller, D. K., Thornberry, N. A., Yamin, T. & Nicholson, D. W., (1996) CPP32/Apopain is a Key Interleukin 1 Beta Converting Enzyme-like Protease Involved in Fas-mediated Apoptosis. J. Biol. Chem. 271(4), 1841-1844. (**Exhibit 28**);
29. Schiestl, R. H. & Gist, R. D., (1989) High Efficiency Transformation of Intact Yeast Cells Using Single Stranded Nucleic Acids as a Carrier. Curr. Genet. 16, 339-346 (**Exhibit 29**);
30. Seilheimer, B., Schachner, M., (1987) Regulation of Neural Cell Adhesion Molecule Expression on Cultured Mouse Schwann Cells by Nerve Growth Factor. The EMBO Journal. 6(6), 1611-

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1616 (**Exhibit 30**);

31. Song, W.-J., Tkatch, T., Baranauskas, G., Ichinohe, N., Kitai, S. T., Surmeier, D. J. (1998) Somatodendritic Depolarization-Activated Potassium Currents in Rat Neostriatal Cholinergic Interneurons Are Predominately of the A Type and Attributable to Coexpression of Kv4.2 and Kv4.1 Subunits. J. Neurosci. 18(9), 3124-3137 (**Exhibit 31**).
32. Smith, R. A. & Baglioni, C., (1987) The Active Form of Tumor Necrosis Factor Is a Trimer. J. Biol. Chem. 262(15), 6951-6954 (**Exhibit 32**);
33. Stefanis, L., Troy, C. M., Qi, H., Shelanski, M. L. & Greene, L. A., (1998) Caspase-2 (Nedd-2) Processing and Death of Trophic Factor-Deprived Pcl2 Cells and Sympathetic Neurons Occur Independently of Caspase-3 (CPP32)-Like Activity. J. Neurosci. 18(22), 9204-9215 (**Exhibit 33**);
34. Taglialatela, G., Robinson, R. & Perez-Polo, J.R., (1997) Inhibition of Nuclear Factor Kappa B (NfkappaB) Actively Induces Nerve Growth Factor-Resistant Apoptosis in PC12 Cells. J. Neurosci. Res. 47, 155-162 (**Exhibit 34**);
35. Tanaka, M., Suda, T., Takahashi, T. & Nagata, S., (1995) Expression of the Functional Soluble Form of Human Fas Ligand in Activated Lymphocytes. The EMBO Journal. 14(6), 1129-1135 (**Exhibit 35**);
36. Tewari, M., Quan, L. T., O'Rourke, K., Desnoyers, S., Zeng, Z., Beidler, D. R., Poirier, G. G., Salvesen, G. S. & Dixit, V. M., (1995) Yama/CPP32beta, A Mammalian Homolog of Ced-3, is a CrmA-Inhibitable Protease that Cleaves the

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Death Substrate Poly(ADP-Ribose) Polymerase. Cell 81, 801-809 (**Exhibit 36**);

37. Vojtek, A. B., Hollenberg, S. M. & Cooper, J. A., (1993) Mammalian Ras Interacts Directly with the Serine/Threonine Kinase Raf. Cell 74, 205-214 (**Exhibit 37**);
38. Weiner, M. P., Felts, K. A., Simcox, T. G. & Braman, J. C., (1993) A Method for the Site-directed Mono- and Multi-mutagenesis of Double-stranded DNA. Gene 126, 35-41 (**Exhibit 38**).

Each of the above-listed publications is listed again on the accompanying PTO Form 1449 (**Exhibit A**).

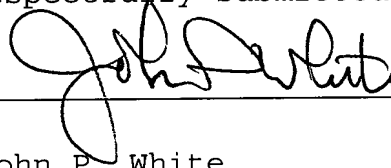
Applicant requests that the Examiner review the publications and make them of record in the subject application.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

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If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

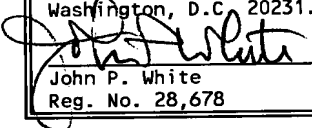
Respectfully Submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner for Patents,  
Washington, D.C. 20231.



John P. White  
Reg. No. 28,678

12/29/99  
Date